

PATENT/Docket No. PC22004B
Appl. No. 10/761,636
Filing Date: January 21, 2004
Reply to Office action of July 1, 2005

REMARKS/ARGUMENTS

In the Office Action date mailed 7/1/2005 Claim 9 was objected as being a substantial duplicate of claim 3. Claim 9 is now canceled and the objection is moot.

Claim rejections were made under 35 USC § 112, first paragraph, as follows:

Claims 1 and 3-11, as well as claims 13-18 were rejected under this provision. Without attempting to recite all the reasons for rejection a summary is that the claims were not definite enough and it would require undue experimentation to determine exactly what 13-monosaccharide 5-oxime avermectins and in what amounts are claimed by the application. Reference to In re Wands factors. The breath of the claims was considered too broad given the examples provided.

Applicant responds here to these arguments with two approaches. First the claims are broad because there is no art reference to disclose the invention and it does not require undue skill to simply substitute various 13-monosaccharide 5-oxime avermectins to utilize the invention. However for the sake of expediency and in order to receive a quick allowance of some claims and without prejudice to refiling continuation applications to unclaimed subject matter, application has amended to claims to one particular 13-monosaccharide 5-oxime avermectin, which is selamectin. In addition, values of selamectin are provided, such that the drug composition would be useful as a topical or spot on application.

The formulations now claimed are selamectin at around 1% to 16% w/v, and praziquantel at around 0.5-10%w/v, in a veterinarily acceptable carrier, diluent or adjuvant suitable for topical application or spot-on application. Thus the claims now clear present no issues of breath or need for experimentation. Anything within or close to these amounts of drugs are included in the claim, provided the diluent or adjuvant is suitable for topical administration.

Claim rejections were made under 35 USC § 112, second paragraph, as follows:

Claims 6 and 12-18 were rejected under 35 USC § 112, second paragraph as being indefinite. Claims included parenthetical phrases leaving ambiguity and uncertainty. Applicant was invited to remove the parenthesis. Claim 13 was considered indefinite because it referred to "treatment and prophylaxis" rather than either treatment or prophylaxis. The amended claims now remove any such uncertainty.

Claim rejections were made under 35 USC § 103a, as follows:

Claims 1-12 and 19 were rejected under Harvey (WO 98/06407) in view of Lukas et. al. (US 2002/0028780). Examiner asserts Harvey teaches various amounts of praziquantel can be combined with macrolide anthelmintics selected from various avermectins and milbemycins, although praziquantel combined with selamectin is not specifically disclosed by Lukas. Examiner also states that Lukas teaches various avermectins that can be prepared for topical or spot-on use, and administered to a dog or cat (page 1, column 2 – page 2, column 1). Examiner then concludes it would be obvious to

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combine a teaching about praziquantel with a teaching about selamectin to create applicant's invention. These teachings however are not suitable for combining because they are each directed toward different problems and there is no art suggestion in the art to create a prima facie case of obviousness.

The reason for this is that while avermectins may be known as useful for topical or spot on applications, praziquantel is not and has not ever been disclosed either by itself or in combination, to be useful in topical administrations of the drug. No one reasonably skilled in the art would use praziquantel topically nor is there any suggestion in the art to use it topically. All of the art cited referring to praziquantel discloses its use as an "oral drench." This is an oral application of the drug. It is a very different thing to take drug intended for oral use and then learn it can be applied effectively in an topical or spot on manner. The fact that selamectin or other avermectin like drugs are applied topically is not relevant to an analysis of the patentability of the claims. Selamectin by itself is not being claimed here.

It may be that "drench" sounds like a topical administration and but in this field and to one ordinarily skilled in the art, the references cited refer to oral administrations not topical. For example if one looks at the web site for, for example MORAG, the Australian Pesticides & Veterinary Medicines Authority, Manual of Requirements and Guidelines for veterinary applications, one will see in volume 2 that an example of a "Major formulation change" section 21 is "where the formulation has been changed significantly to accommodate a new application method/use pattern (eg changing from a wettable powder to an emulsifiable concentrate; **changing from an oral drench to a topical pour-on dosage form**). Bold added here. It should thus be clear that such a change is major and would require a major effort to get something like that approved. Thus it is neither obvious nor would one be motivated to seek to combine a topical delivered drug like selamectin with a drug like praziquantel.

There are additional reasons why one ordinarily skilled in the art would not consider combining praziquantel with selamectin. Praziquantel is known to be relatively insoluble and there is nothing to suggest that a solvent system could be found which would allow topical application of, either selamectin with a drug like praziquantel by itself or these two actives. Nor is there any art to suggest that a solvent system useful for selamectin would be suitable for praziquantel.

Lukas et al. said to teach avermectin or milbemycin with DEGMME or DPGMME in the formulation, including ethanol or isopropanol also misses the point here. It is not the avermectin that is difficult to formulate, it is the praziquantel. And it is the combination of these two actives that is claimed here.

The Examiner asserts the art teaches that praziquantel may be combined with "any other compound of the avermectin group"; reference to Harvey (WO 98/06407), however, selamectin is different from other avermectins in that, unlike the other avermectins, it has no commercial livestock activity. Selamectin is used as a low volume topical spot-on to kill fleas in companion animals. This is very unlike the oral drench for sheep, cattle and goats taught by WO 98/06407 and the skilled person would be unlikely to combine these teachings.

On page 2, 4th paragraph of the application, as filed, we set out the desirable attributes for a topical formulation for administration to companion animals. Those attributes include: a topical application for administration to companion animals such as cats and dogs, (especially for treatment for the control of flea, heartworm and tapeworm infestation) efficacy; persistence of efficacy; low volume; cosmetically acceptable; convenient; need for small number of applications for broad spectrum parasite

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control; compliant treatment; safe; suitable pharmacokinetic profile; suitable transdermal flux profile; rapid rate of onset; low dose of active ingredient(s); cutaneous tolerability; and stability on storage.

The string of citations below are all taken from the US Dist. Court Decision *SmithKline Beecham Corp. v. Apotex Corp.* on March 31, 2005, decided March 31, 2005 filed and entered March 31. Internal citations are also provided.

"A person of ordinary skill in the art is . . . presumed to be one who thinks along the line of conventional wisdom in the art and is not one who undertakes to innovate, whether by patient, and often expensive, systematic research or by extraordinary insights" *Am. Cyanamid Co.*, 774 F.3d at 454.

"Two requirements must be satisfied for a claim to be obvious in light of prior art. *Brown & Williamson Tobacco Corp. v. Phillip Morris, Inc.*, 229 F.3d 1120, 1124-25 (Fed. Cir. 2000). First, there must be a reason, suggestion, or motivation to modify the teachings of the prior art reference to the claimed invention. *Sibia Neurosciences, Inc.*, 225 F.3d at 1356.

"The purpose of this requirement is to prevent a hindsight-based inquiry into obviousness, which the Federal Circuit has repeatedly instructed is inappropriate. *See, e.g., id.* at 664-65; *In re Dembiczak*, 175 F.3d 994, 999 (Fed. Cir. 1999) ("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references."). Whether there was a reason, suggestion, or motivation to modify the teachings of prior art is a question of fact. *McGinley v. Franklin Sports, Inc.*, 262 F.3d 1339, 1351 (Fed. Cir. 2001).

"Second, the prior art must suggest to a person of ordinary skill in the art that the allegedly obvious process, if undertaken, would have a reasonable likelihood of success. *Brown & Williamson Tobacco Corp.*, 229 F.3d at 1125; *In re Dow Chem. Co.*, 837 F.2d at 473. This does not require "absolute predictability of success," but rather a reasonable expectation that the process would be successful. *In re*

O'Farrell, 853 F.2d 894, 903 (Fed. Cir. 1988). An assertion that, in light of the prior art, it would have been "obvious to try" the allegedly obvious process is insufficient to meet this requirement. *Ecolochem, Inc. v. S. Cal. Edison Co.*, 227 F.3d 1361, 1374 (Fed. Cir. 2000).

Here there is nothing in the art to suggest the combination of these two ingredients for the indicated or for any other purpose. Indeed the art surrounding praziquantel teaches away from the use claimed here. It was previously used as an oral drench. Here a novel nonobvious combination and use are described and claimed.

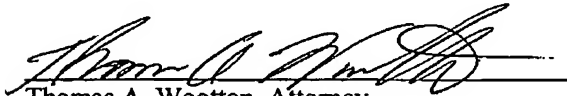
There is nothing in the art to suggest that a formulation combining selamectin and praziquantel could be created that would be efficacious; persistent; low volume; cosmetically acceptable; convenient; etc. etc. no reason to even try this combination in fact much less expect it to work well.

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Given the amendments provided here application believes the claims are now in condition for allowance. Applicants believe that the claims are in order for allowance, early notice of which is requested. If Examiner has any questions concerning this application, Examiner is invited to contact the below-signed attorney. Please charge any payment or credit any overpayment to Deposit Account 21-0718.

Respectfully submitted,


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